Standardized virus detection by NAT

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until 30 September 2015

[2]Institut für Qualitätskontrolle in derVirusdiagnostik (IQVD), Berlin
since 01 October 2015

[3]Gesellschaft für Biotechnologische Diagnostik (GBD) mbH, Berlin

[4]INSTAND e.V. - Gesellschaft zur Förderung der Qualitätssicherung in medizinischen Laboratorien e.V., Düsseldorf

Collaborating Centers of International Consortium for Blood Safety (ICBS), New York and Düsseldorf

JCTLM Members' and Stakeholders's Meeting
BIPM, Sèvres
30 November – 01 December 2015

Outline

Infectious diseases – challenges
01 December – World AIDS Day

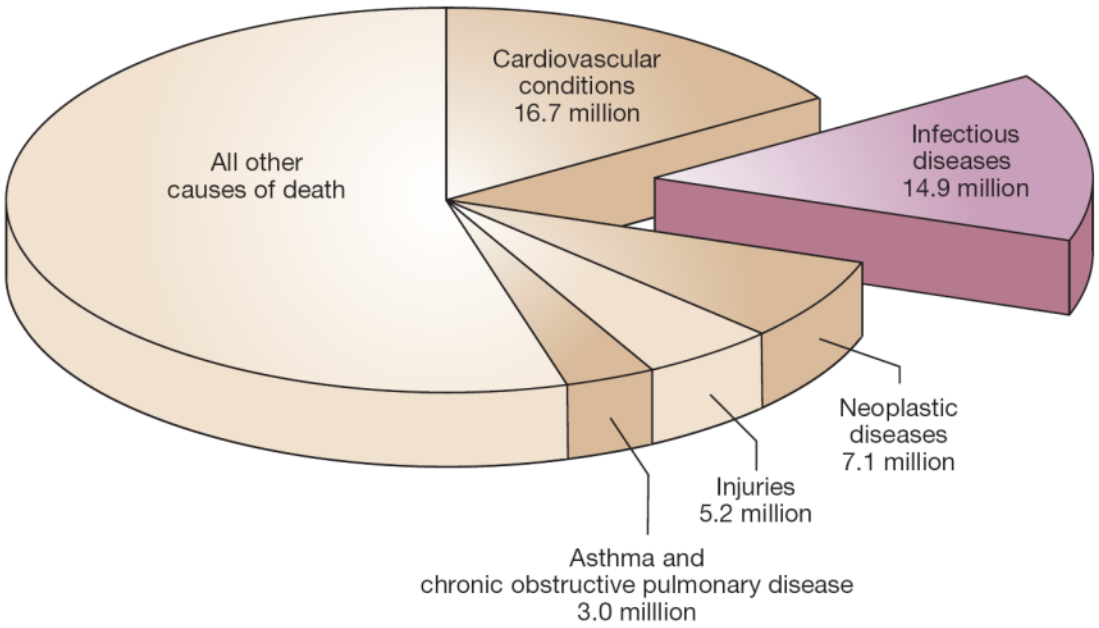
External quality assessment schemes – INSTAND

Quantitative genome detection of HIV-1 (RNA)

Quantitative genome detection of cytomegalovirus

Benefits of Quality Controlled and Standardized Diagnostics

Leading Causes of Death per Year Worldwide

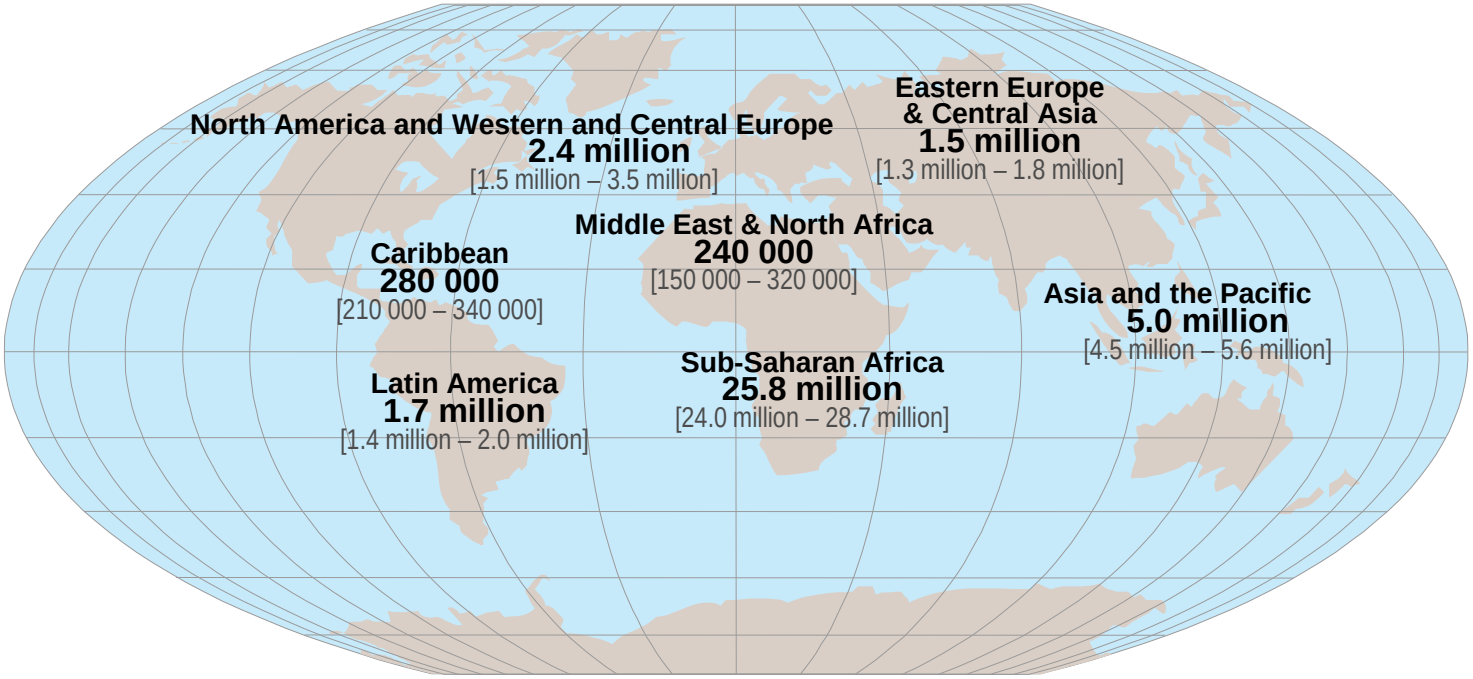


Infectious diseases	Annual deaths (million)
Respiratory infections	3.96
HIV/AIDS	2.77
Diarrhoeal diseases	1.80
Tuberculosis	1.56
Vaccine-preventable childhood diseases	1.12
Malaria	1.27
STDs (other than HIV)	0.18
Meningitis	0.17
Hepatitis B and C	0.16
Tropical parasitic diseases	0.13
Dengue	0.02
Other infectious diseases	1.76

Figure 2 Leading causes of death worldwide. About 15 million (>25%) of 57 million annual deaths worldwide are the direct result of infectious disease. Figures published by the World Health Organization (see http://www.who.int/whr/en and ref. 7).

Morens, D. M., Folkers, G. K. and Fauci, A. S., Nature, 430, p. 242, 2004

Adults and children estimated to be living with HIV | 2014



Total: 36.9 million [34.3 million – 41.4 million]

UNAIDS

About 5,600 new HIV infections a day in 2014

- **About 66% are in Sub Saharan Africa**
- **About 600 are in children under 15 years of age**
- **About 5,000 are in adults aged 15 years and older, of whom:**
  - **almost 48% are among women**
  - **about 30% are among young people (15-24)**

UNAIDS

Treatment Costs for HIV/AIDS Patients in Germany

(O. Hamouda, Robert Koch Institute, 2012, personal communication)

	per **1** HIV/AIDS patient (in Germany, 2012)	per **50,000** HIV/AIDS patients (in Germany, 2012)
Annual costs for HAART*	20,000 EUR	1,000,000,000 EUR
Accumulated costs for 50 years under HAART*	1,000,000 EUR	------
Annual costs for medical consultation, hospitalization and rehabilitation	2,000 EUR	100,000,000 EUR

*HAART: Highly active antiretroviral therapy with
Reverse Transkriptase-Inhibitoren (NRTI und NNRTI)
Protease-Inhibitoren (PI)

Global Dimension of Infections with HIV, HBV, HCV and TB

People living with HIV/AIDS infection:	**37 million**
People who have been infected with HBV:	**2,000 million**
People with chronic HBV infection:	**350 million**
People infected with HCV:	**180 million**
People with chronic HCV infection:	**130 million**
People infected with TB	**2,000 million**

Dimensions of Coinfections - Global

HIV/AIDS and hepatitis C:	**4-5 Mio.**
HIV/AIDS and chronic hepatitis B:	**2-4 Mio.**
HIV/AIDS and tuberculosis:	**16 Mio.**

WHO, 2007; Friedland, 2007; Alter, 2006

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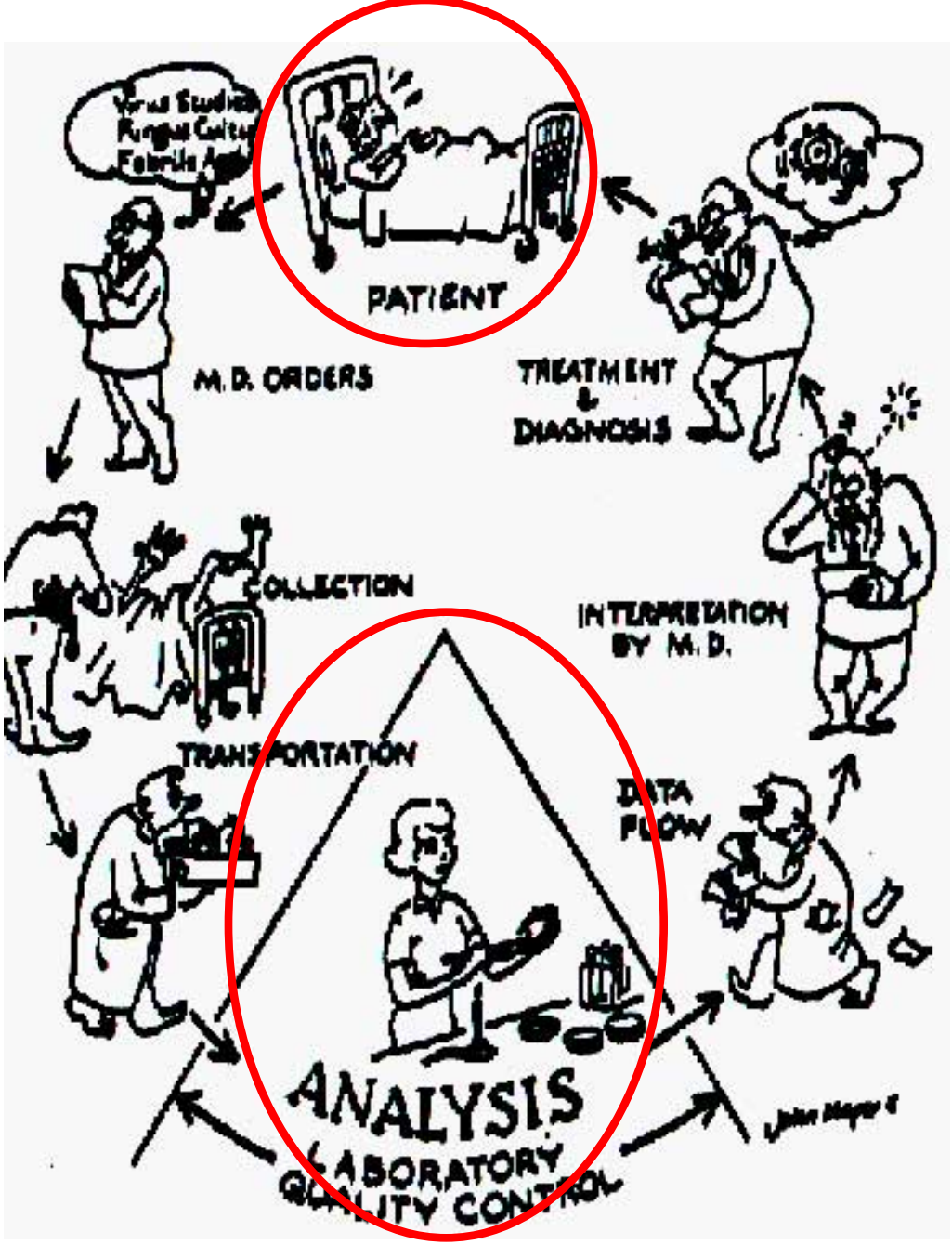
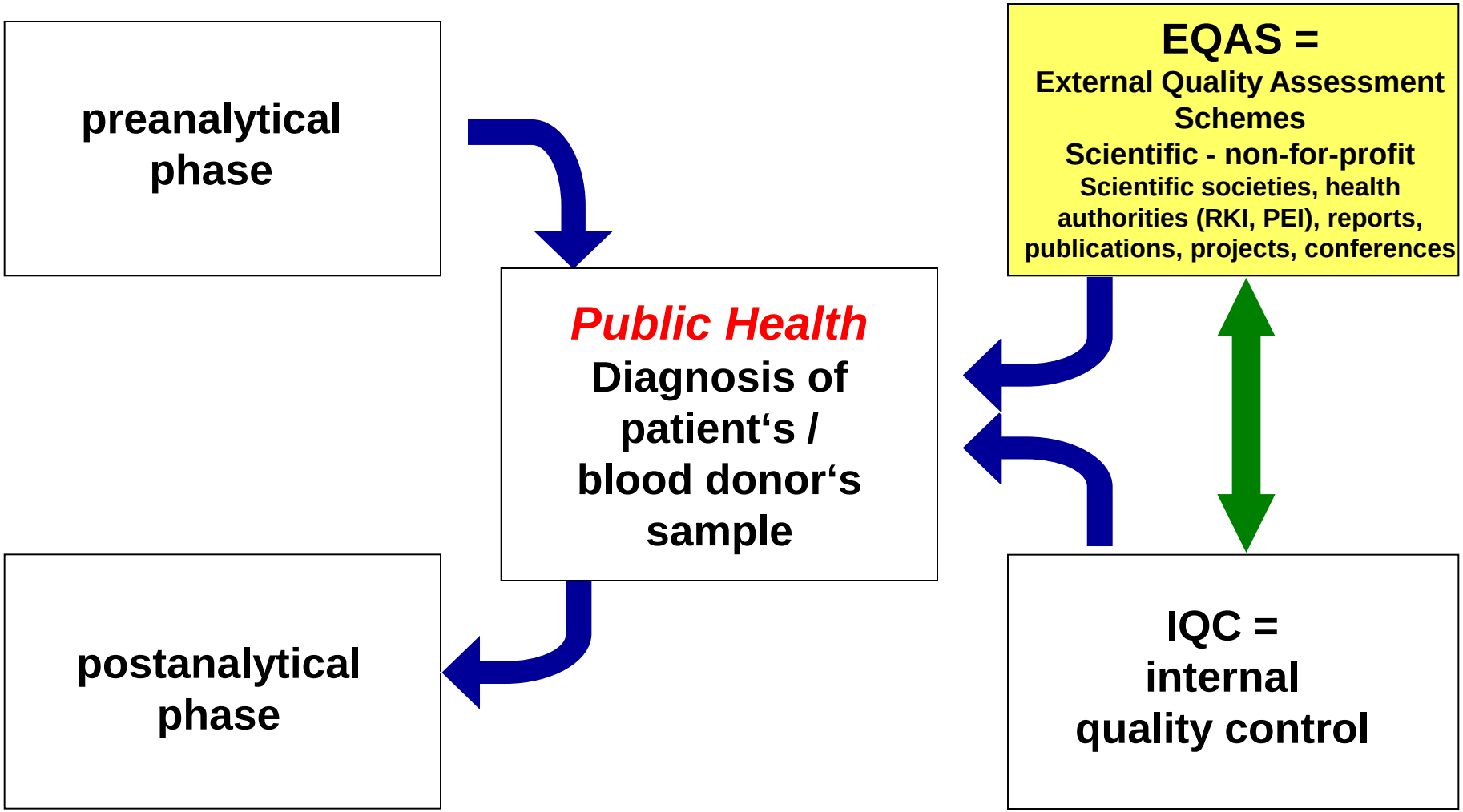


Quality Management
in Medical Laboratories
ISO 9000:2000
Wemmie Elsenga
http://www.epbs.net/brussels/brussels03_elsenga.htm

The Role of Quality Control for Public Health and Quality Improvement of Diagnostics and Blood Safety



The Role of Quality Control for Public Health and Quality Improvement of Diagnostics and Blood Safety

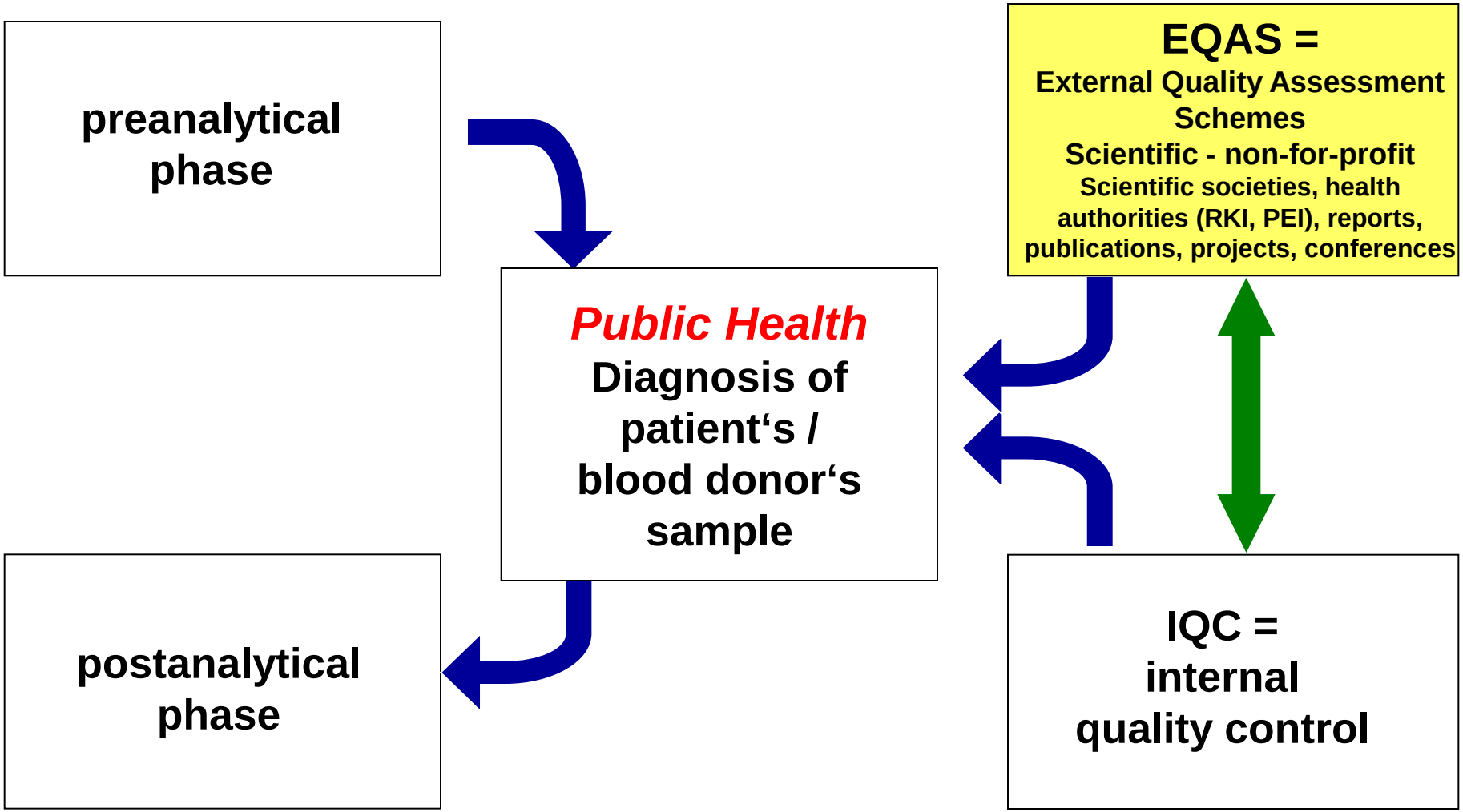
preanalytical phase

Ringversuche = EQAS
External Quality Assessment Schemes
Scientific - non-for-profit
Scientific societies, health authorities (RKI, PEI), reports, publications, projects, conferences

postanalytical phase

IQC = internal quality control

The Role of Quality Control for Public Health and Quality Improvement of Diagnostics and Blood Safety



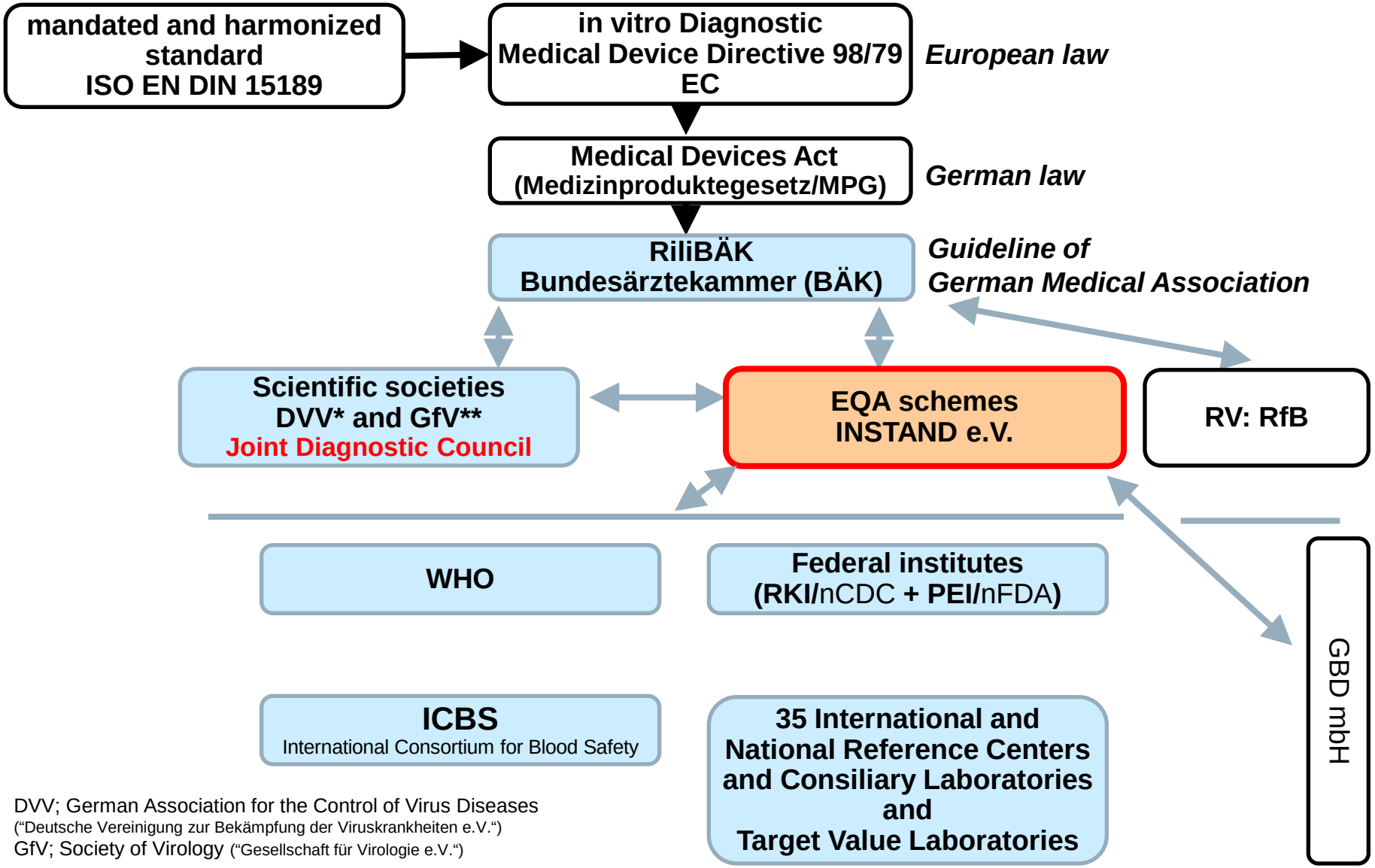
RiliBÄK - Guidelines of the German Medical Association on Quality Assurance in Medical Laboratory Testimg

New Guideline for Quality Assurance of the German Medical Association (RiliBÄK)

-> mandatory for all medical laboratories in Germany

Section A **Fundamental requirements** for quality assurance	Effective since 1 April 2008
Specific Section B 1 Quantitative analyses in laboratory medicine ***- internal QA*** ***- external QA***	Effective since 1 April 2008
Specific Section B 2 Qualitative analyses in laboratory medicine ***- internal QA*** ***- external QA***	Effective since 1 July 2011
Specific Section B 3 Direct detection and characterization of pathogens ***- internal QA*** ***- external QA***	Effective: 1 June 2015
Specific Section B 4 Analyses of ejaculate ***- internal QA*** ***- external QA***	Effective since 1 July 2011
Specific Section B 5 Molecular- and cytogenetic analyses ***- internal QA*** ***- external QA***	Effective since 1 October 2011

Quality Assurance in Virus Diagnostics



* DVV; German Association for the Control of Virus Diseases ("Deutsche Vereinigung zur Bekämpfung der Viruskrankheiten e.V.")

** GfV; Society of Virology ("Gesellschaft für Virologie e.V.")

INSTAND EQA Schemes

Clinical chemistry

Virtual EQA schemes

POCT

Molecular diagnostics

Pharmaceutic and drugs

Mycology

Trace elements

Parasitology

>350

Programs

Haematology

Virology (65 progs)

Immunohaematology

Bacterial genome detection

Haemostasis

Bacteriology / serology

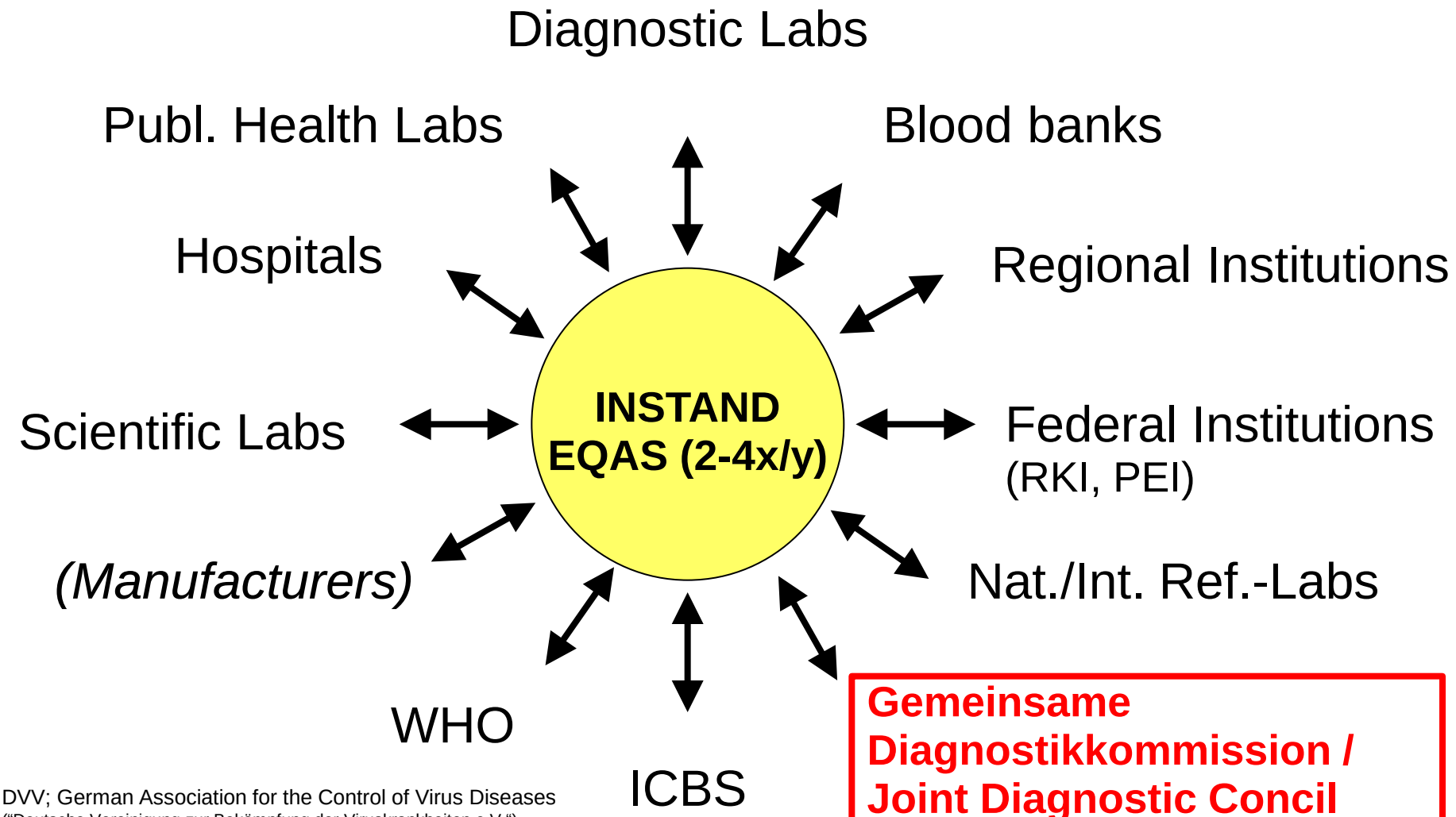
Autoimmune diseases

Special EQA schemes (hormones etc.)

INSTAND EQA Schemes (65 Schemes) in Virus Immunology and Genome Detection 2015

Serology and Antigen Detection		Virus Genome Detection and Typing	
HIV-1/2	Herpes simplex Viruses	**HIV-1 (RNA)** **HIV-2 (RNA)**	Measles Rubella Mumps Viruses
HIV-1 p24 Ag	Varicella Zoster Virus	HIV-1 Resistance + Tropism	Adenoviruses
HTLV-1/2	Epstein Barr Virus	Hepatitis A Virus	Norovirus Rotavirus
Hepatitis A Virus	Resp. Sync. Virus Ag	Hepatitis B Virus + Genotyping + Resistance	Coronavirus
Hepatitis B Virus, Prg. I	Influenza A and B Ag +A/H1N1 pdm 2009 +A/H5N1+A/H7N9	Hepatitis C Virus + Genotyping + Resistance	Enteroviruses + Enterovirus (WHO/RKI)
Hepatitis B Virus, Prg. II	Rubella Virus Measles Virus Mumps Virus	Hepatitis D Virus Hepatitis E Virus	Human Rhinoviruses Resp. Syncytial Virus Hum. Metapneumovirus Parainfluenza viruses
Hepatitis C Virus	TBE Virus	**Cytomegalovirus** + Resistance	Influenza A and B Ag +A/H1N1 pdm 2009 +A/H5N1+A/H7N9
Hepatitis D Virus	Hantavirus	Epstein-Barr Virus	BK Virus JC Virus
Hepatitis E Virus	Dengue Virus	Herpes simplex Viruses	Dengue Virus West Nile Virus Chikungunya Virus
Parvovirus B19	Rabies Virus	Varicella Zoster Virus	Hum. Papilloma Viruses
Cytomegalovirus	BSE (PrPsc) (2002-2007)	Parvovirus B19	Rabies Virus

INSTAND EQAS Network – Virus Diagnostics



Gemeinsame Diagnostikkommission / Joint Diagnostic Concil von/of DVV* and GfV**

* DVV; German Association for the Control of Virus Diseases ("Deutsche Vereinigung zur Bekämpfung der Viruskrankheiten e.V.")

** GfV; Society of Virology ("Gesellschaft für Virologie e.V.")

INSTAND Target Value Laboratories (in total: 35)

• O. Adams	Universitätsklinikum Düsseldorf
• A. Baillot	Niedersächsisches Landesgesundheitsamt, Hannover
• S. Becker / M. Eickmann	Philipps Universität Marburg, Nat. Konsiliarlab. Filoviren
• C.-T. Bock / M. Höhne	Robert Koch-Institut, Berlin; Nat. Konsiliarlab. Noroviren
• M. Chudy / S.A. Baylis / J. Kreß	**Paul-Ehrlich-Institut, Langen, WHO CC**
• S. Diedrich	Robert Koch-Institut, Berlin; NRZ Poliomyelitis und Enteroviren Regionales Referenzlabor der WHO/EURO für Poliomyelitis
• U. Dittmer / S. Ross / M. Roggendorf	**Universitätsklinik Essen; NRZ HCV; Nat. Konsiliarlab. Tollwut**
• G. Dobler	Institut für Mikrobiologie der Bundeswehr, München
• Ch. Drosten / A.-M. Eis-Hübinger	Universität Bonn
• J. Eberle / L. Gürtler	**Ludwig-Maximillians-Universität München, Max-von-Pettenkofer Institut**
• G. Enders / M. Enders	**Labor Enders, Stuttgart**
• A. Gessner / B. Schmidt / J. Wenzel	Universität Regensburg; Nat. Konsiliarlab. HAV und HEV
• S. Günther / J. Schmidt-Chanasit / P. Emmerich	Bernhard-Nocht-Institut, Hamburg; NRZ trop. Infektionserreger, WHO CC
• G. Harms-Zwingenberger / R. Ignatius	Institut für Tropenmedizin, Berlin
• H.H. Hirsch	Universität Basel, Dept. Biomedizin
• D. Huzly / M. Panning	Universitätsklinikum Freiburg
• G. Jahn / K. Hamprecht	**Universitätsklinikum Tübingen; Nat. Konsiliarlab. CMV**
• A. Karl / K. Frank / K. Gubbe	DRK-Blutspendedienst Ost, Plauen
• O.T. Keppler / H. Rabenau / A. Berger / M. Stürmer	**Universitätsklinikum Frankfurt; NRZ Retroviren**
• D. Krüger / J. Hofmann	**Charité Universitätsmedizin Berlin, CCM;** **Nat. Konsiliarlab.Hantaviren; Labor Berlin – Charité Vivantes GmbH**
• C. Kücherer	Robert Koch-Institut, Berlin
• U.G. Liebert	Universität Leipzig
• A. Mankertz / S. Santibanez	Robert Koch-Institut, Berlin; NRZ Masern, Mumps und Röteln
• T. Mertens / D. Michel	**Universitätsklinikum Ulm; Nat. Konsiliarlab.CMV**
• S. Modrow	Universität Regensburg; Nat. Konsiliarlab. Parvoviren
• T. Müller	Friedrich-Loeffler-Institut, OIE u. Nat. Referenzlab. Tollwut
• S. Nick / H. Scheiblauer	Paul-Ehrlich-Institut, Langen; Prüflabor für IVD
• M. Niedrig	Robert Koch-Institut, Berlin; Nat. Konsiliarlab. FSME
• H. Pfister / U. Wieland / R. Kaiser	**Uniklinik Köln; NRZ Papillom- und Polyomaviren**
• B. Weißbrich	Universität Würzburg; Nat. Konsiliarlab. RSV, Parainfluenzaviren und HMPV
• A. Sauerbrei / P. Wutzler	Universitätsklinikum Jena; Nat. Konsiliarlab. HSV und VZV
• T. Schulz / A. Heim	Medizinische Hochschule Hannover; Nat. Konsiliarlab. Adenoviren
• T. Schulz / W. Puppe / C. Schmitt	Medizinische Hochschule Hannover; Nat. Konsiliarlab. EBV, HHV 6, 7, 8
• B. Schweiger	Robert Koch-Institut, Berlin; NRZ Influenza
• S. Smola, N. Müller-Lantzsch, J. Rissland	**Universitätsklinikum des Saarlandes**
• K. Überla / K. Korn	**Universitätsklinikum Erlangen**
• J. Ziebuhr, D. Glebe / C. Schüttler / W. Gerlich	Universität Gießen; NRZ HBV und HDV

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WHO International Standard HIV-1 RNA

- 1st International Standard for HIV-1 RNA for HIV-1 NAT assays, code 97/656 - established by the ECBS in 1999
- WHO International Standard HIV-1 RNA, 2nd International Standard NIBSC code: 97/650 Instructions for use
  (Version 3.0, Dated 04/03/2008)
- WHO International Standard 3rd HIV-1 International Standard NIBSC code: 10/152 Instructions for use
  (Version 5.0, Dated 23/11/2015)

EQAS for Qualitative PCR (Polymerase Chain Reaction)

HIV

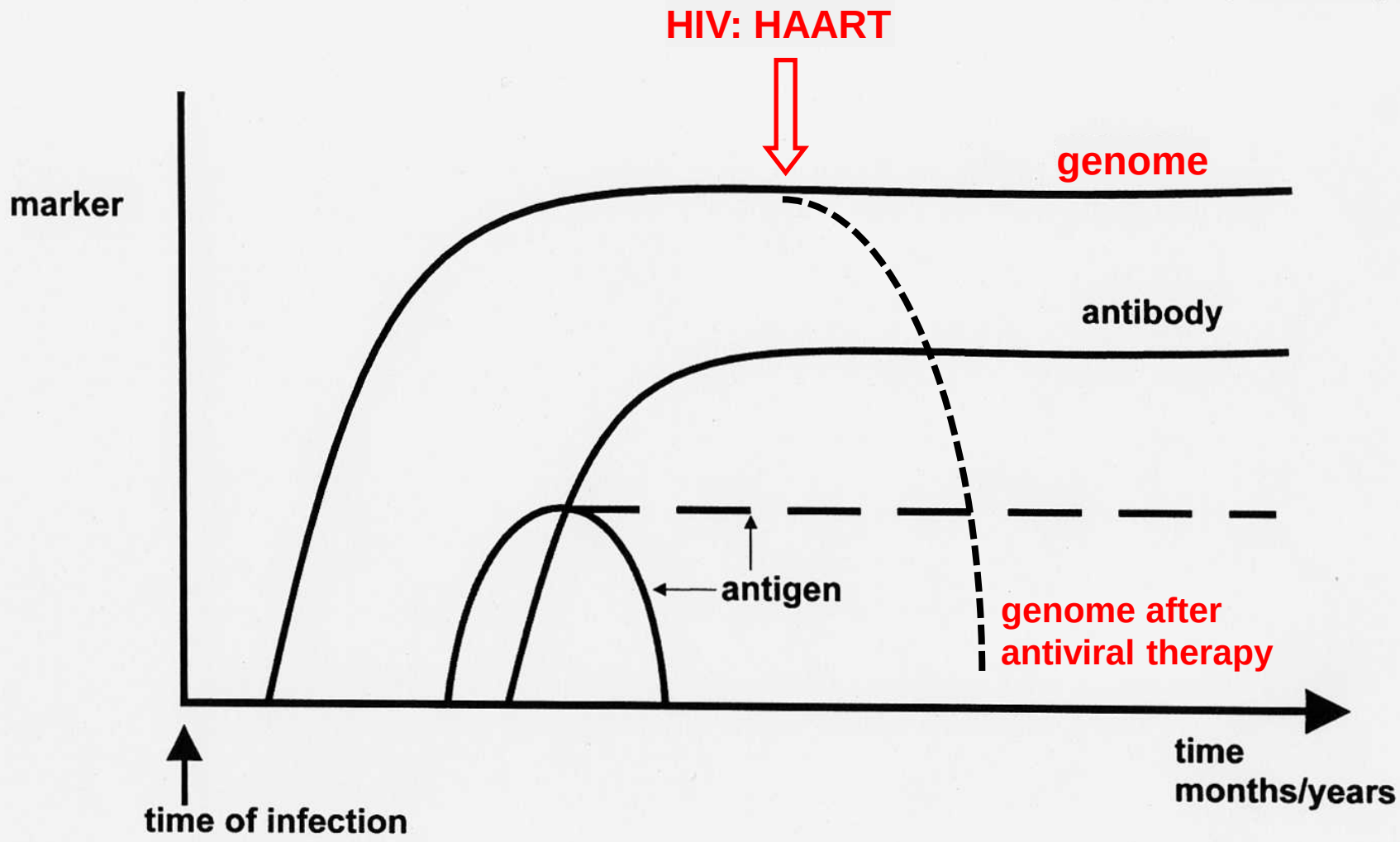
➔

Performance improvement by training

Supporting legal decisons on detection intervals

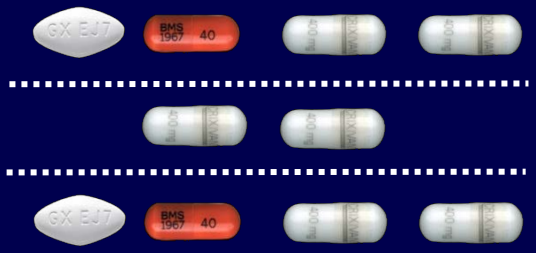
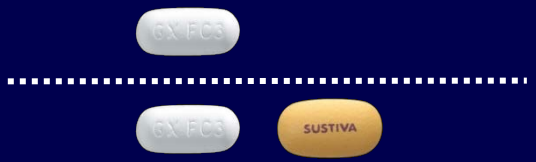
New Guideline for Quality Assurance of the German Medical Association / Neue Richtlinie der Bundesärztekammer zur Qualitätssicherung laboratoriumsmedizinischer Untersuchungen (RiliBÄK)

Generalised course of infection (TTIs)



JB/mm/8nov01(14)
micro/slides/dubai

Simplification of HIV Therapy 1996 - 2006

1996: d4T/3TC/IDV	10 pills, TID	
1998: ZDV/3TC/EFZ	5 pills, BID	
2002: ZDV/3TC/EFV	3 pills, BID	
2004: TVD or EPZ /EFV	2 pills, QD	
2006: ATRIPLA	1 pill, QD	

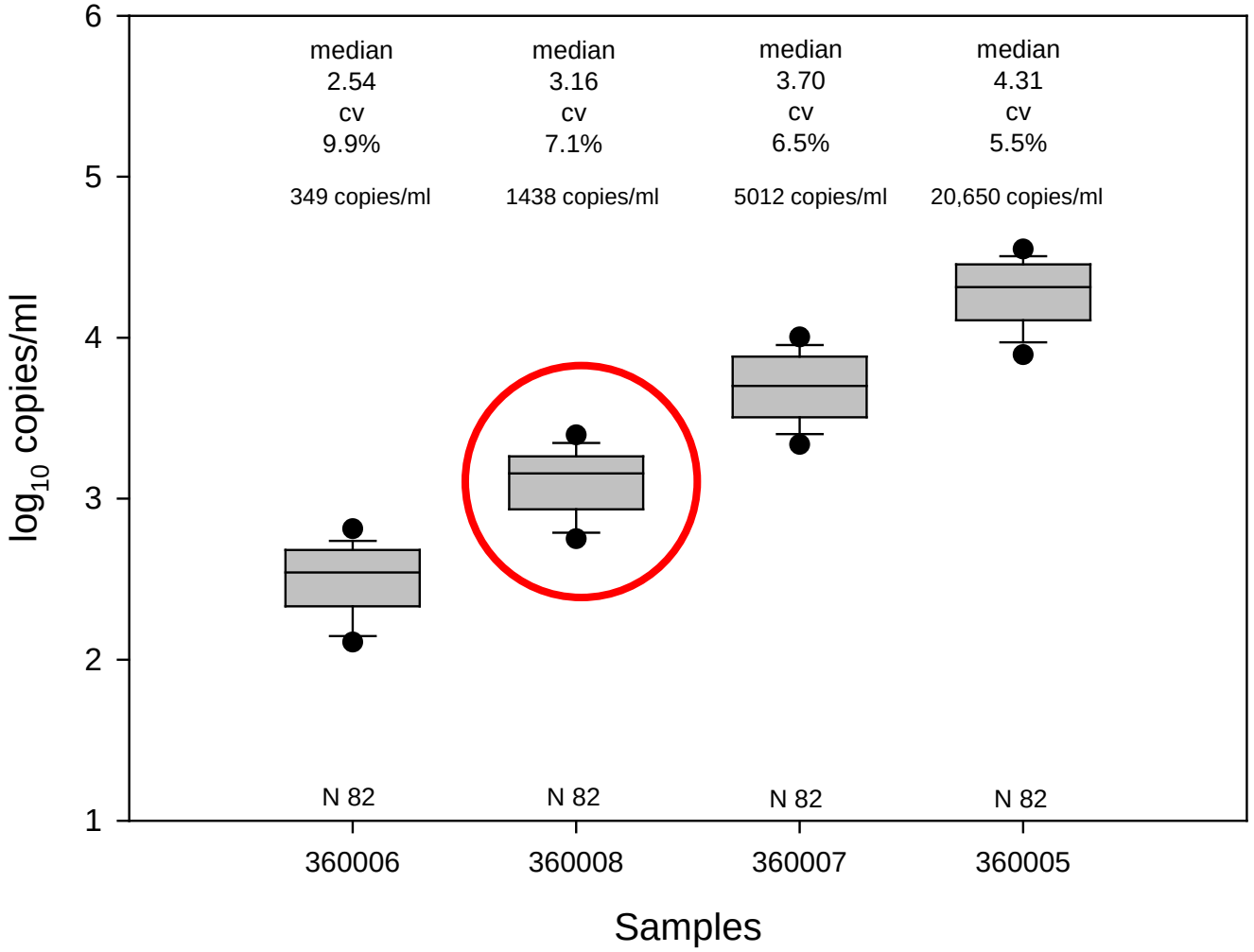
INSTAND-EQA schemes for quantitative HIV-1 genome detection for mimicing therapy monitoring

- quantitative genome determination
  - basis for therapy monitoring
- decrease of >=log_{10} copies/ml within 1 month
  - indicator for antiviral efficacy
  - if not: antiviral resistance?
- target
  - get viral load below level of detection
- example for EQA scheme
  dilution series of one and the same HIV stock:
  - 1 : 200 x 10^7
  - 1 : 50 x 10^7
  - 1 : 12,5 x 10^7
  - 1 : 3,125 x 10^7

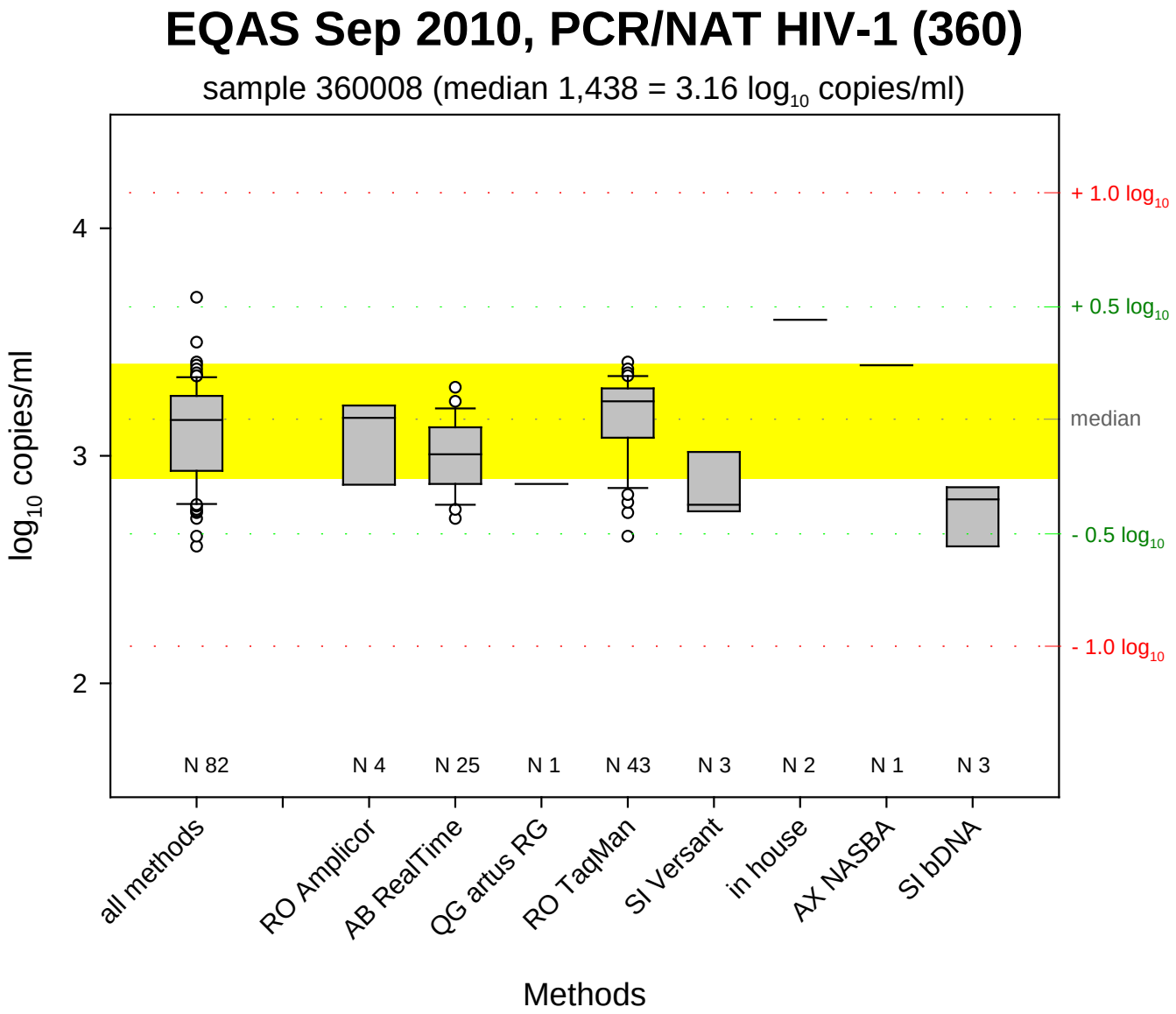
INSTAND-EQAS for HIV-1: Sample Dilution Series

EQAS Sep 2010, PCR/NAT HIV-1 (360)

all methods (4 samples: dilution factors: 1:200x10^7, 1:50x10^7, 1:12.5x10^7, 1:3.125x10^7)



INSTAND-EQAS for HIV-1: Sample Dilution Series



within succes rate

+/- 1.0 $\log_{10}$ = 100.0% (82/82)

+/- 0.5 $\log_{10}$ = 96.3% (79/82)

+/- 0.25 $\log_{10}$ = 72.0% (59/82)

RiliBÄK Specific Section B 3:
Direct Detection and Characterization of Pathogens
- Quantitative Detection of Nucleic Acid of HIV-1

Table B 3-2a
Evaluation thresholds for external quality assurance of nucleic acid detection of pathogens transmitted by blood/plasma/serum

1 No.	2 Analyte	3 Acceptable deviation of log10 value of participant from log10 target value of EQA scheme	4 Range of valitity in respect to column 3			5 Traget value of EQA scheme	6 Frequency of EQA scheme
			from	to	unit		
1	CMV DNA	-0,8 to+0,8	5 000	5 000 000	IU/mL	Target value	2x/year
2	HBV DNA	-0,6 to+0,6	500	5 000 000	IU/mL	Target value	2x/year
3	HCV RNA	-0,6 to +0,6	500	5 000 000	IU/mL	Target value	2x/year
4	HIV-1 RNA	-0,6 to +0,6	500	5 000 000	copies/mL	Target value	2x/year

INSTAND EQAS: Virus Genome Detection of HIV-1 (RNA)

Main EQA Scheme (360) and Training Program (382)

Properties of samples for the main EQA scheme "Virus Genome Detection - HIV-1 (RNA)" (360) September 2014		
Sample No.	**Sample source**	**Dilution** Dilution factor: 4 or multiple of 4
360069	negative plasma pool of healthy blood donors	-----
360070 = 360071*,$	highly purified HIV-1 isolate (subtype B) from a patient with HIV/AIDS	1 : 8 000 000*,$
360071 = 360070*,$		1 : 8 000 000*,$
360072*		1 : 125 000*

Properties of samples for the EQA scheme "Virus Genome Detection - HIV-1 (RNA) - Training Program" (382) September 2014		
Sample No.	**Sample source**	**Dilution** Dilution factor: 4 or multiple of 4
382005*,$	highly purified HIV-1 isolate (subtype B) from a patient with HIV/AIDS	1 : 8 000 000*,$
382006*		1 : 32 768 000 000*
382007*		1 : 8 192 000 000*
382008*		1 : 512 000 000*

INSTAND EQAS: Virus Genome Detection of HIV-1 (RNA)

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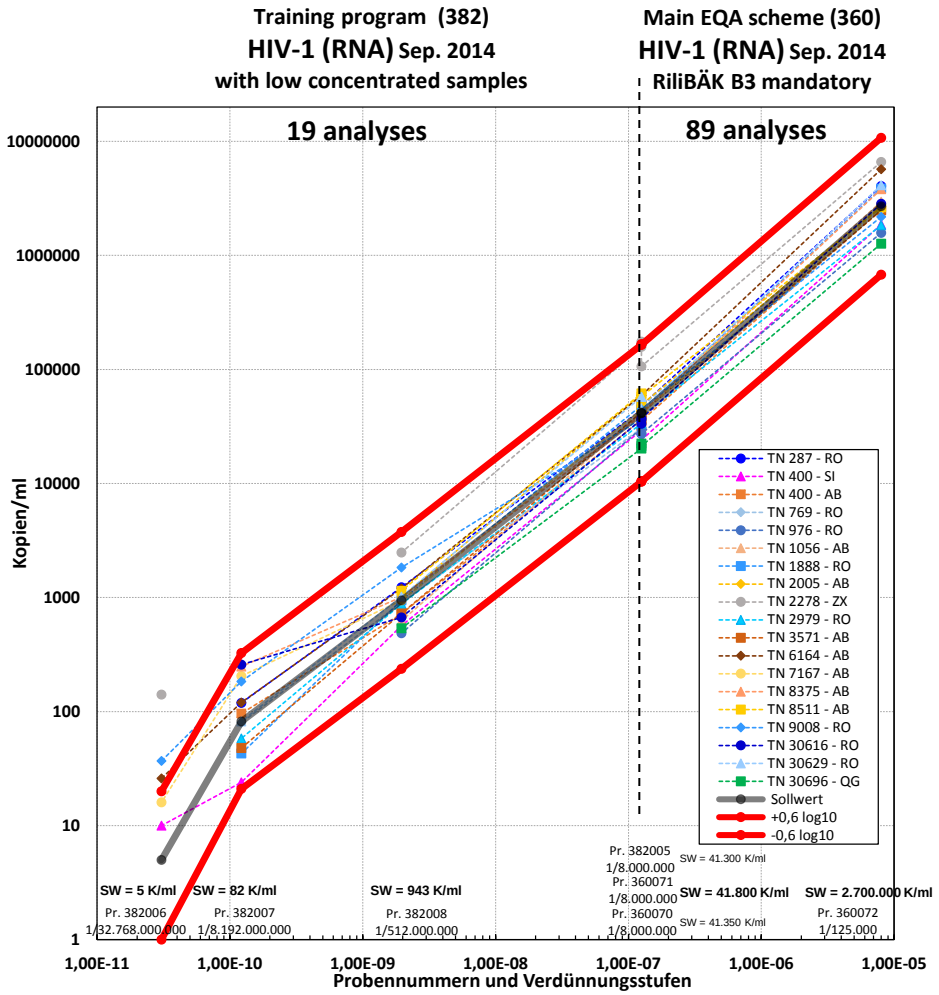


INSTAND EQAs September 2014:
Main EQA "Virusgenome detection - HIV-1 (RNA)" (360)
and
Training program "Virusgenome detection - HIV-1 (RNA)" (382)

results in copies

broken down to individual laboratories having paticipated in both EQA schemes (N=24)

Dilution series of HIV-1 subtype B (highly purified) in plasma

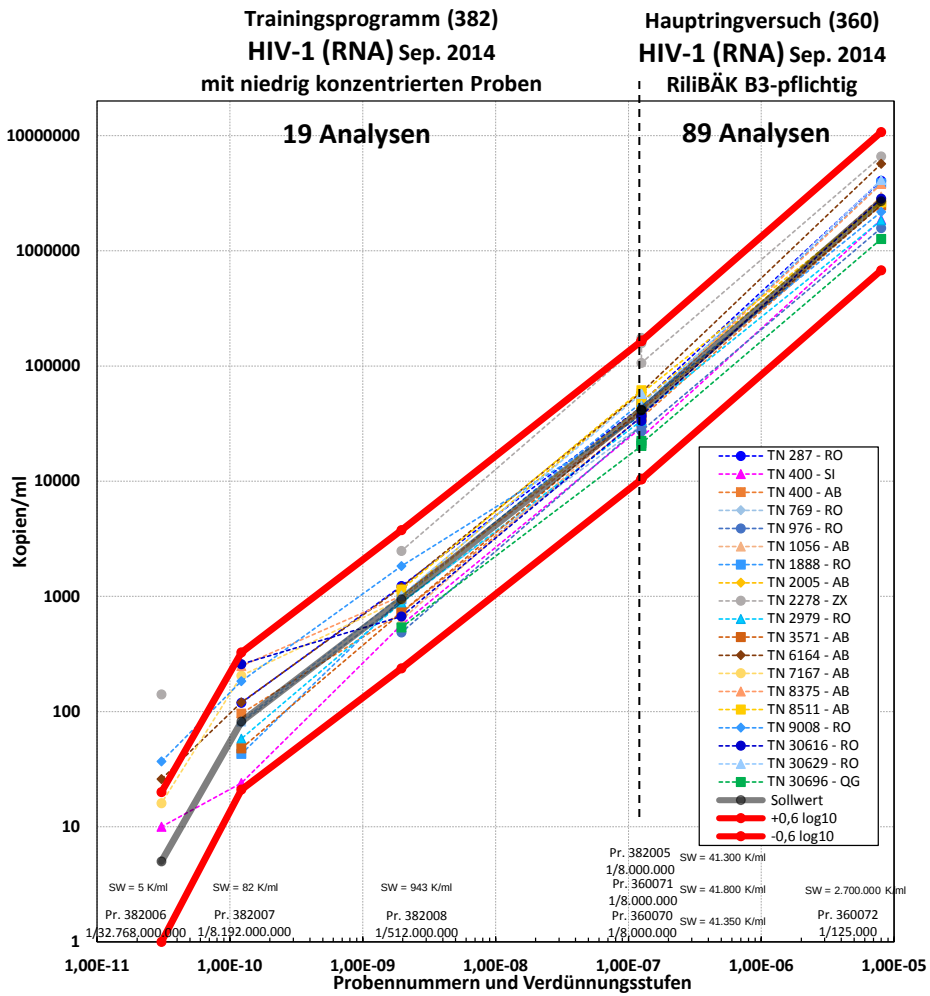
Dilution factor: 4 or multifold of 4

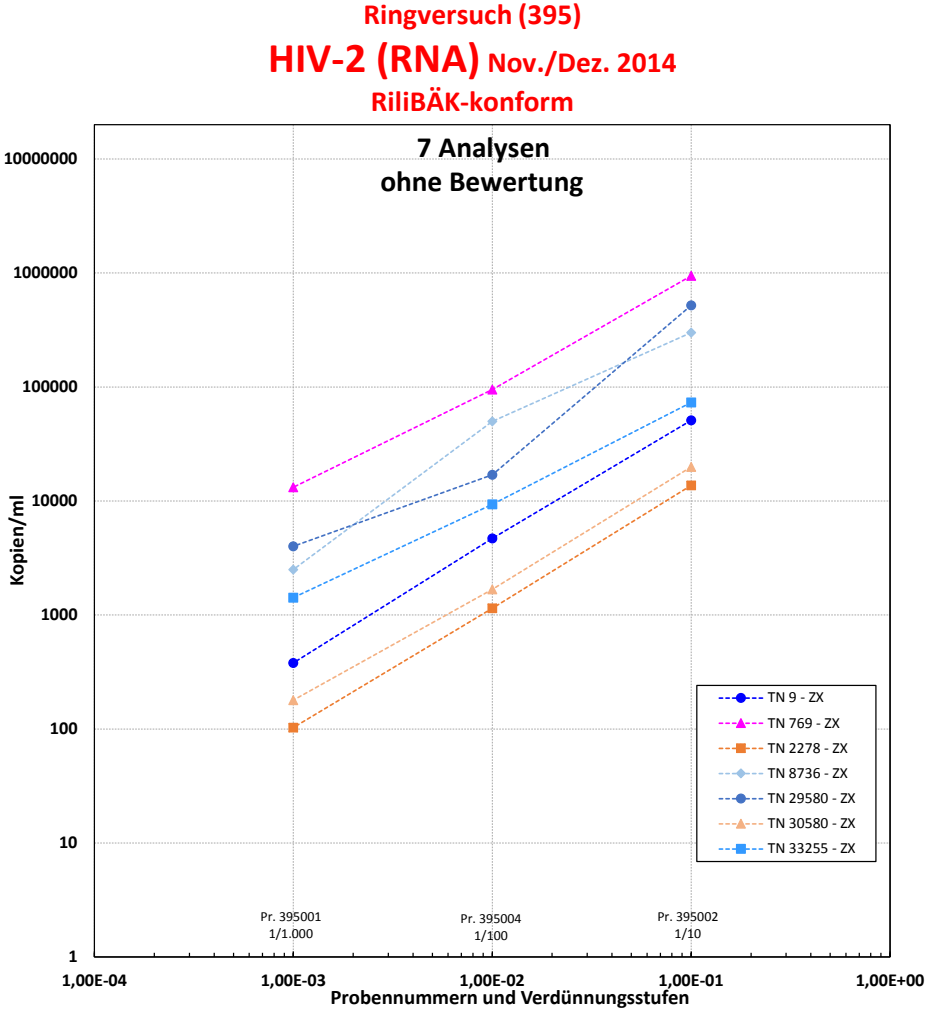
1 : 125.000 - 1 : 32.768.000.000 (2.700.000 - 5 copies/ml)

H. Zeichhardt, O. Donoso Mantke, V. Lindig und H.-P. Grunert, Charité Universitätsmedizin Berlin, CBF, Virologie / INSTAND, Düsseldorf / GBD, Berlin
in Kooperation mit H. Rabenau, NRZ für Retroviren, Universitätsklinikum Frankfurt

INSTAND-RVs: Virusgenom-Nachweis von HIV-1 und HIV-2

Streuung der quantitativen Messergebnisse der INSTAND Ringversuche zum Virusgenom-Nachweis von HIV-1 (RNA) und HIV-2 (RNA)





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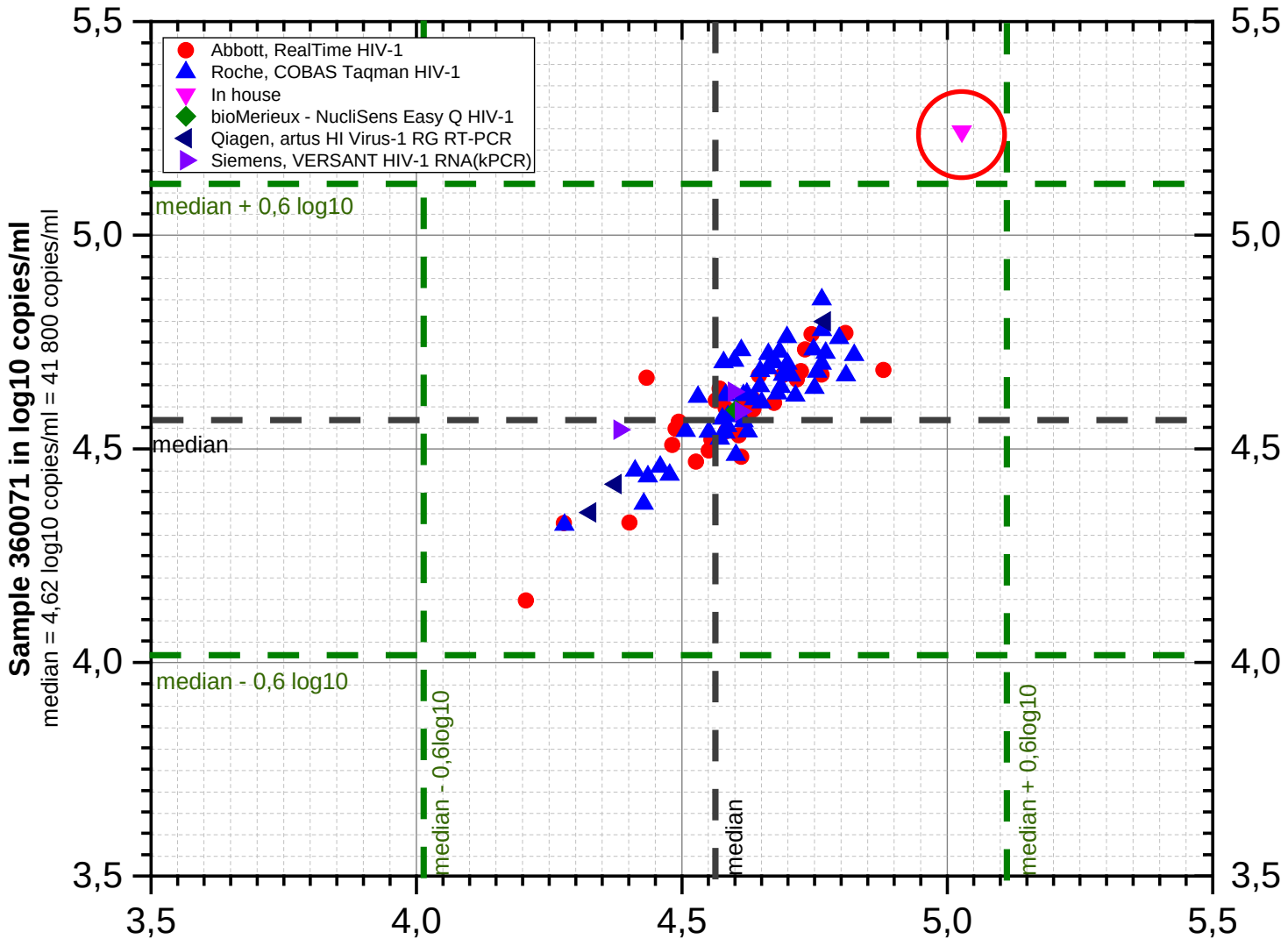
360072*		1 : 125 000*

Properties of samples for the EQA scheme "Virus Genome Detection - HIV-1 (RNA) - Training Program" (382) September 2014		
Sample No.	**Sample source**	**Dilution** Dilution factor: 4 or multiple of 4
382005*,$	highly purified HIV-1 isolate (subtype B) from a patient with HIV/AIDS	1 : 8 000 000*,$
382006*		1 : 32 768 000 000*
382007*		1 : 8 192 000 000*
382008*		1 : 512 000 000*

INSTAND EQAS: Virus Genome Detection of HIV-1 (RNA)

Main EQA Scheme (360) Sep 2014 – Youden plot of samples 360070 vs 360071



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3	HCV RNA	-0,6 to +0,6	500	5 000 000	IU/mL	Target value	2x/year
4	HIV-1 RNA	-0,6 to +0,6	500	5 000 000	copies/mL	Target value	2x/year

INSTAND-EQAS - Virus Genome Detection of CMV

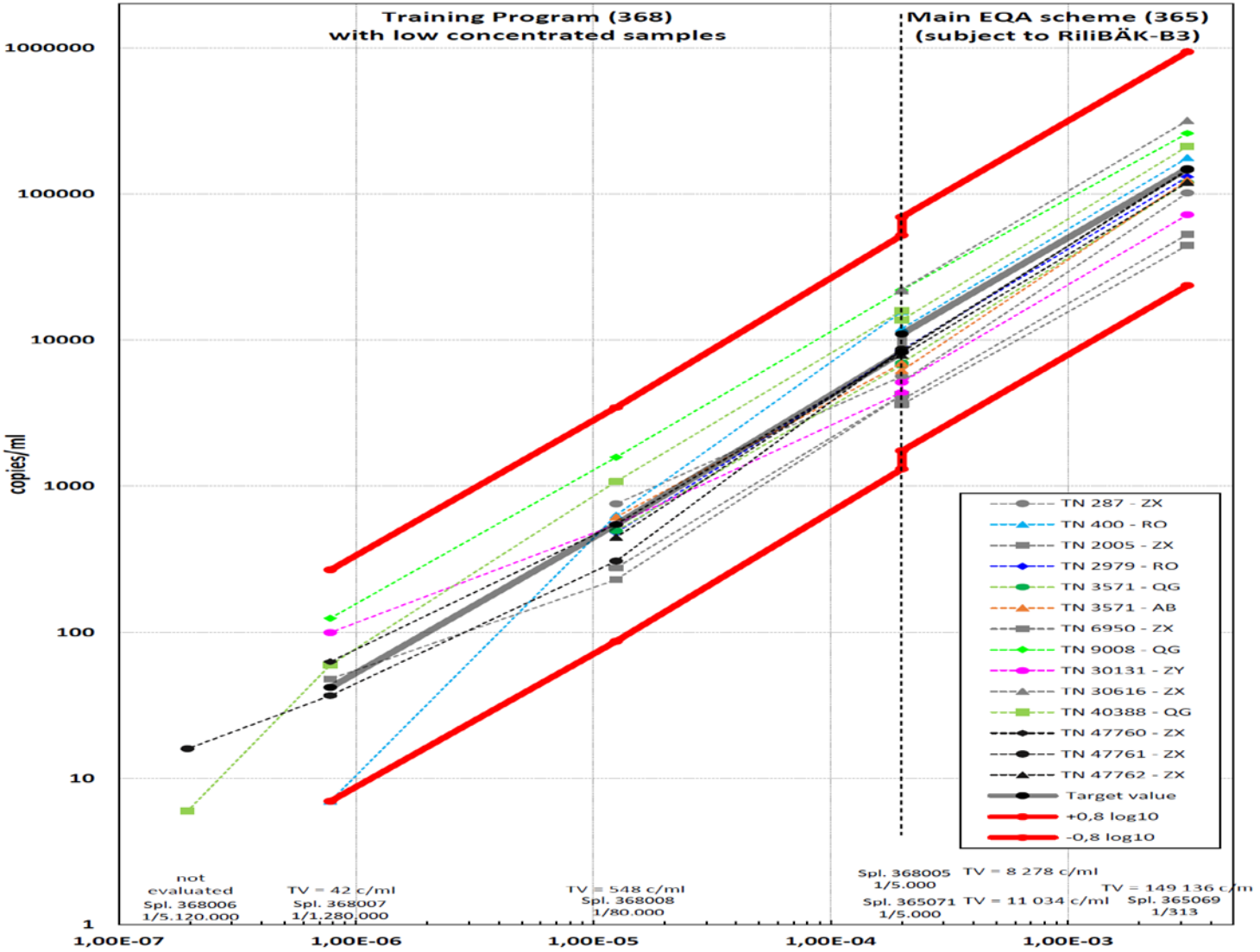
Main-EQA Scheme (365) and Training Program (368) – September 2014

Main EQA scheme (365)		
Sample No.	**Sample source**	**Dilution** **Dilution factor: 4 x Y**
365069*	plasma pool of healthy blood donors spiked with a lysate of CMV infected cells (isolate of a patient)	1 : 313*
365070 = 365072	negative plasma pool of healthy blood donors	----
365071*,$	plasma pool of healthy blood donors spiked with a lysate of CMV infected cells (isolate of a patient)	1 : 5 000*,$
365072 = 365070	negative plasma pool of healthy blood donors	----

Training Program (368)		
Sample No.	**Sample source**	**Dilution** **Dilution factor: 4 x Y**
368005*,$	plasma pool of healthy blood donors spiked with a lysate of CMV infected cells (isolate of a patient)	1 : 5 000*,$
368006*		1 : 5 120 000*
368007*		1 : 1 280 000*
368008*		1 : 80 000*

INSTAND-EQAS - Virus Genome Detection of CMV

Main-EQA Scheme (365) and Training Program (368) – September 2014 – Copies/ml



Digital PCR (dPCR) for Quantitative Detection of Human Cytomegalovirus

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EMRP
European Metrology Research Programme
Programme of EURAMET
The EMRP is jointly funded by the EMRP participating countries within EURAMET and the European Union

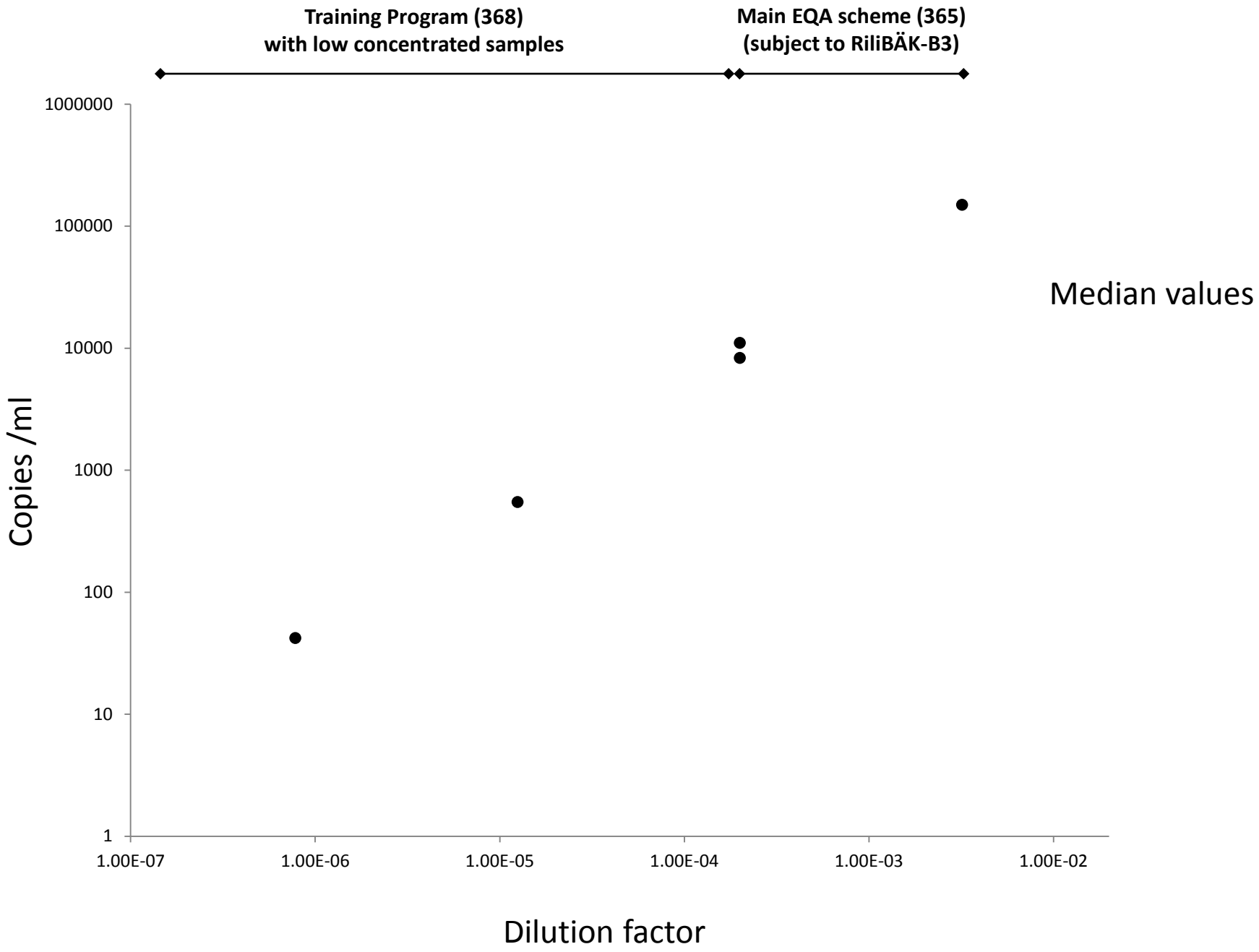
EURAMET
European Association of National Metrology Institutes

- Cooperation of INSTAND with Charité Berlin within
  JRP HLT08 INFECT-MET
  Metrology for monitoring infectious diseases, antimicrobial resistance, and harmful micro-organisms

JRC, Geel, EU	**LGC, Teddington, UK**	**NIB, Ljubljana, Slovenia**
Heinz Schimmel	Helen Parks	Jana Zell
Maria Karczmarczyk	Jim Huggett	Jernej Pavšič
Fran van Heuverswyn	Claire Bushell	Mojca Milavec
	Alison Devonshire	
	Carole Foy	
	Denise O'Sullivan	

- Results of 3 laboratories using dPCR
  in the INSTAND-EQA schemes - Virus Genome Detection of CMV

  Main-EQA Scheme (365) and Training Program (368) – September 2014


Training Program (368)
with low concentrated samples
Main EQA scheme (365)
(subject to RiliBÄK-B3)
1000000
100000
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10
1
Copies /ml
1.00E-07
1.00E-06
1.00E-05
1.00E-04
1.00E-03
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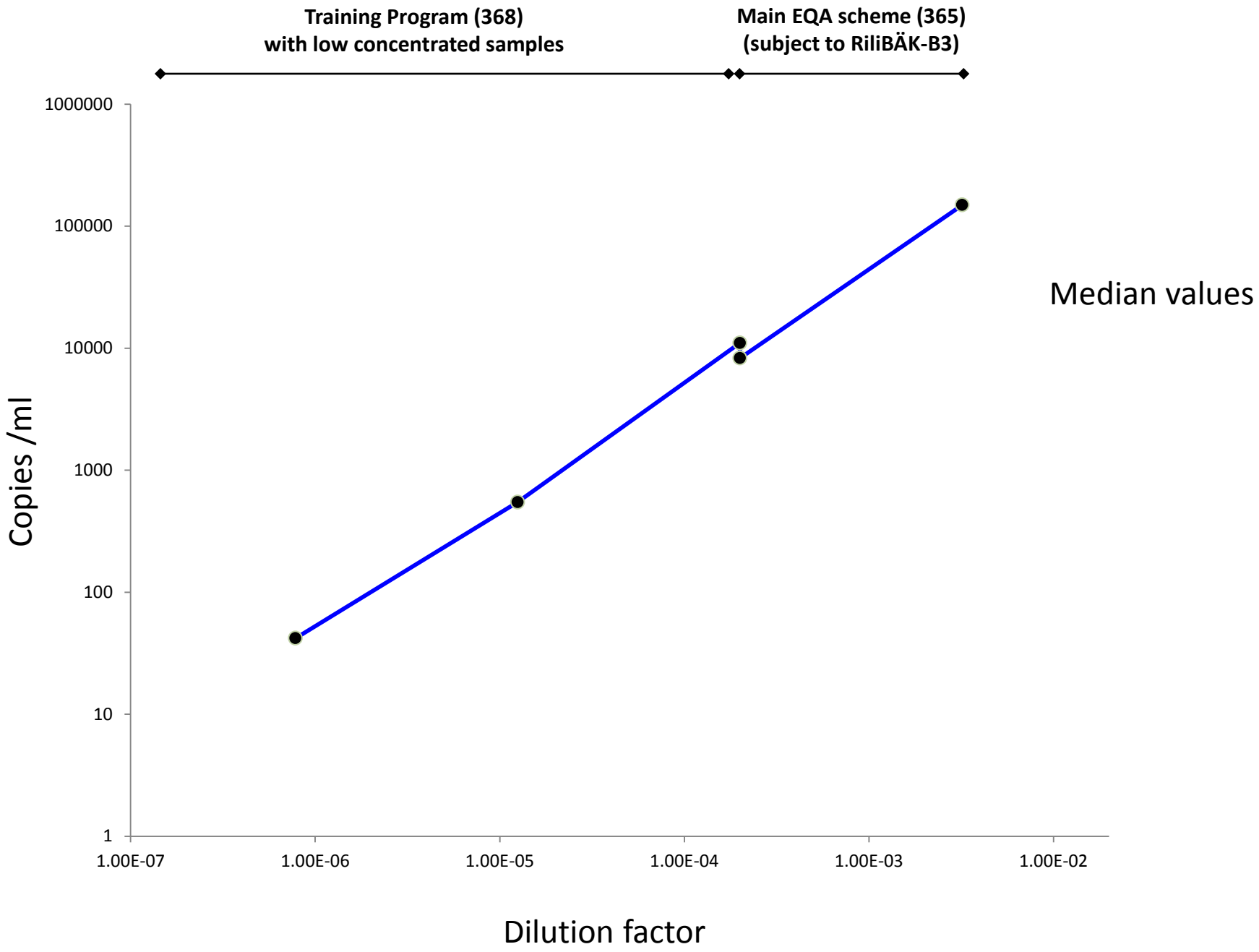
Dilution factor
Median values


Training Program (368)
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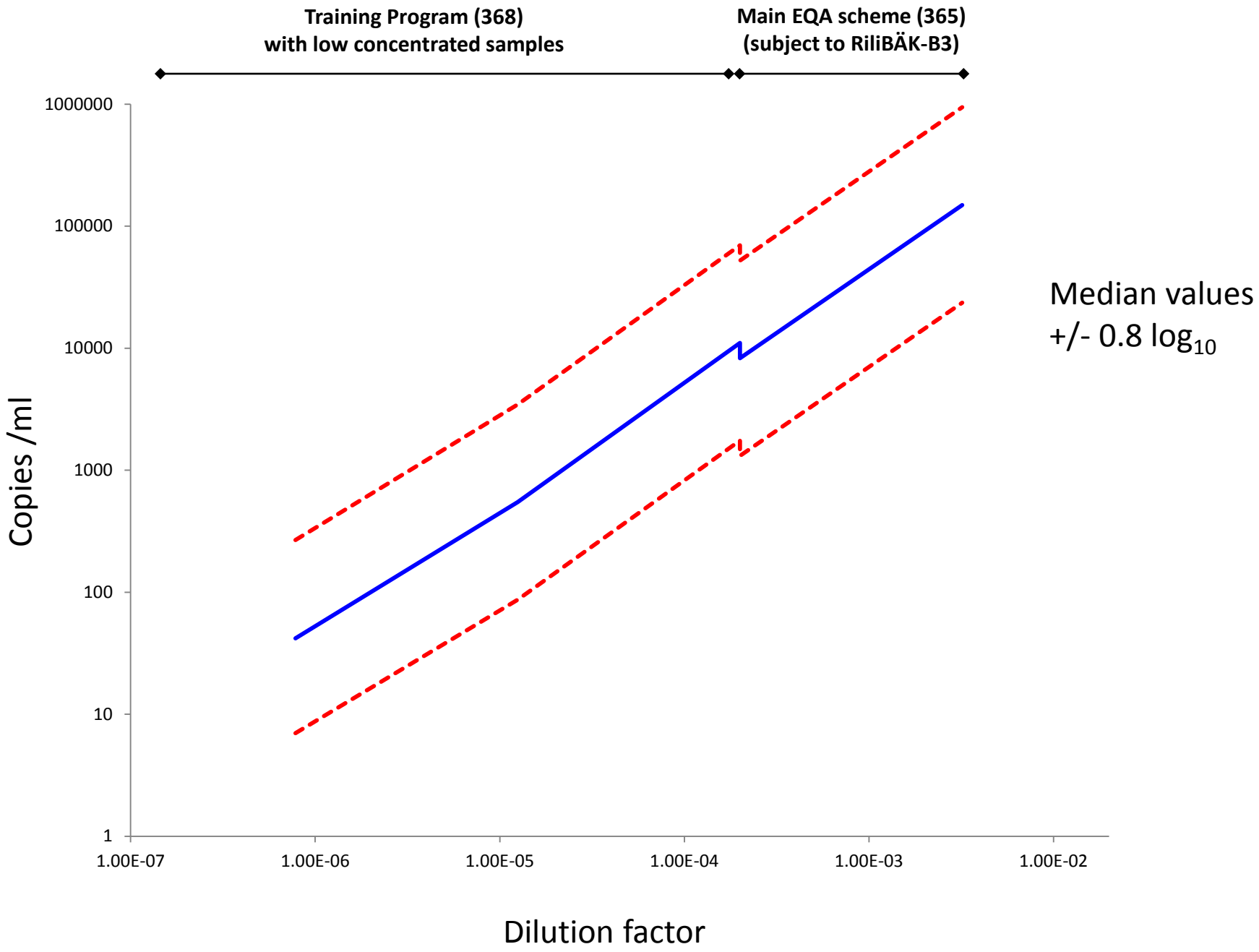
Dilution factor
Median values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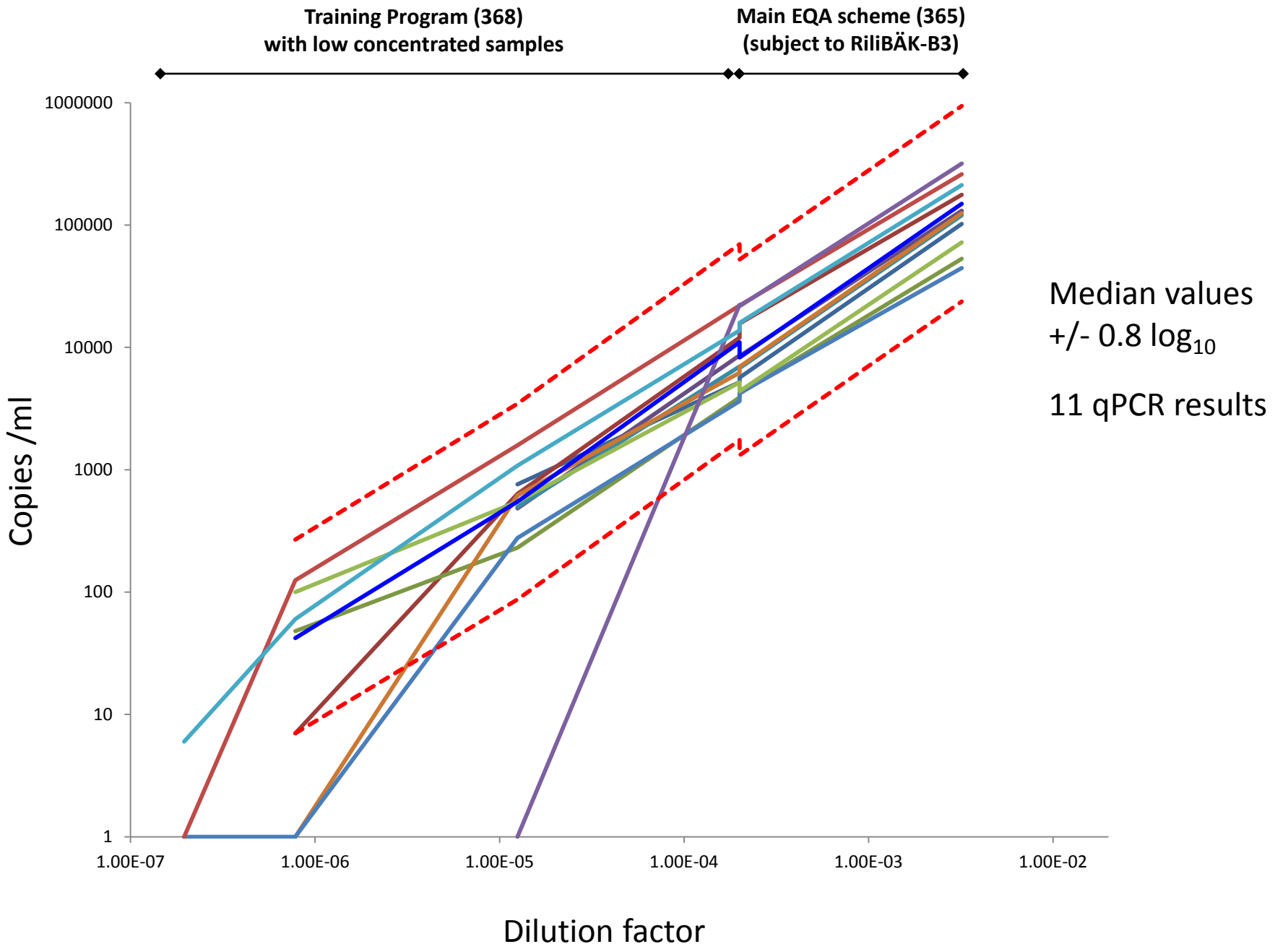
1.00E-02
Dilution factor
Median values
+/- 0.8 log10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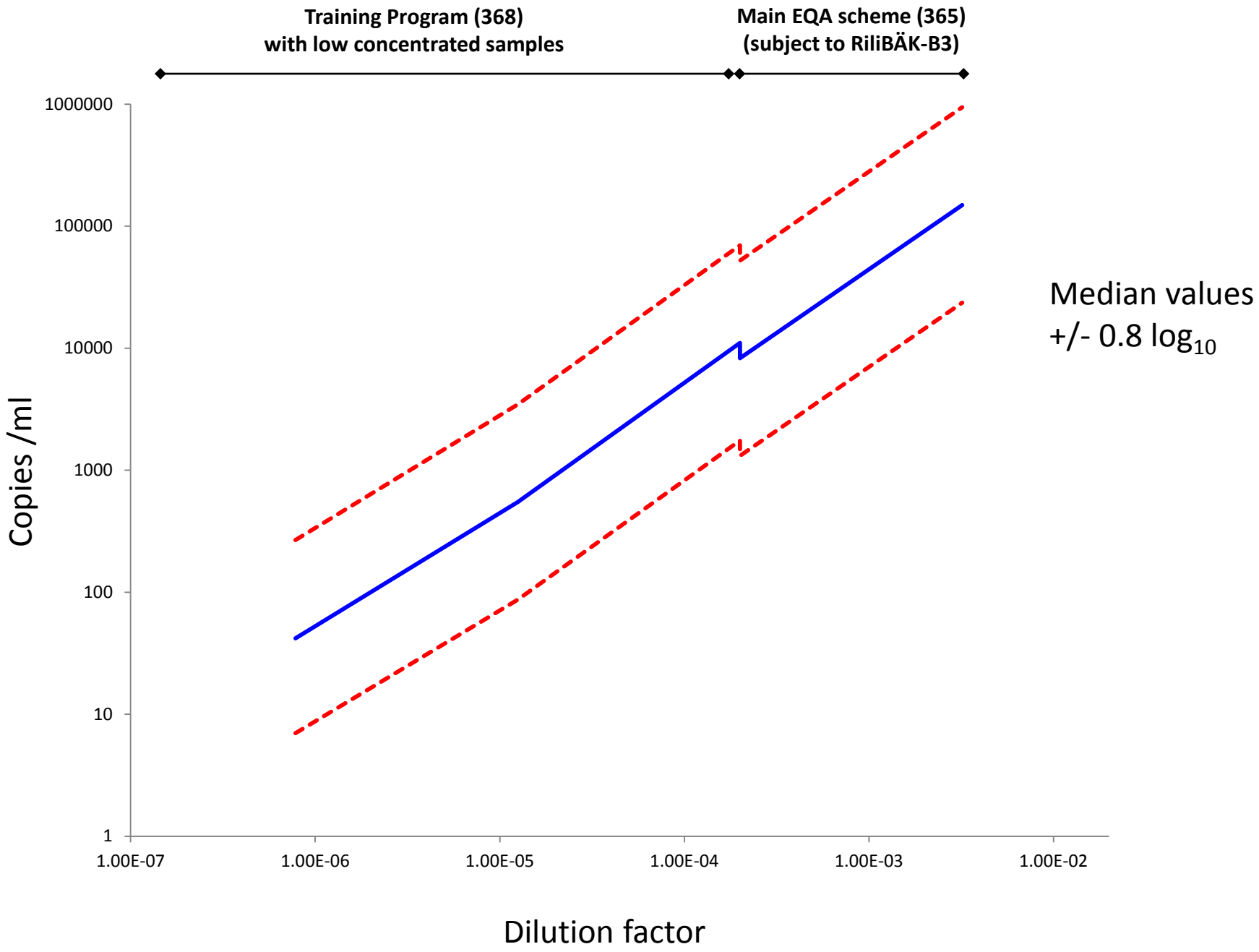
1.00E-02
Dilution factor
Median values
+/- 0.8 log10
11 qPCR results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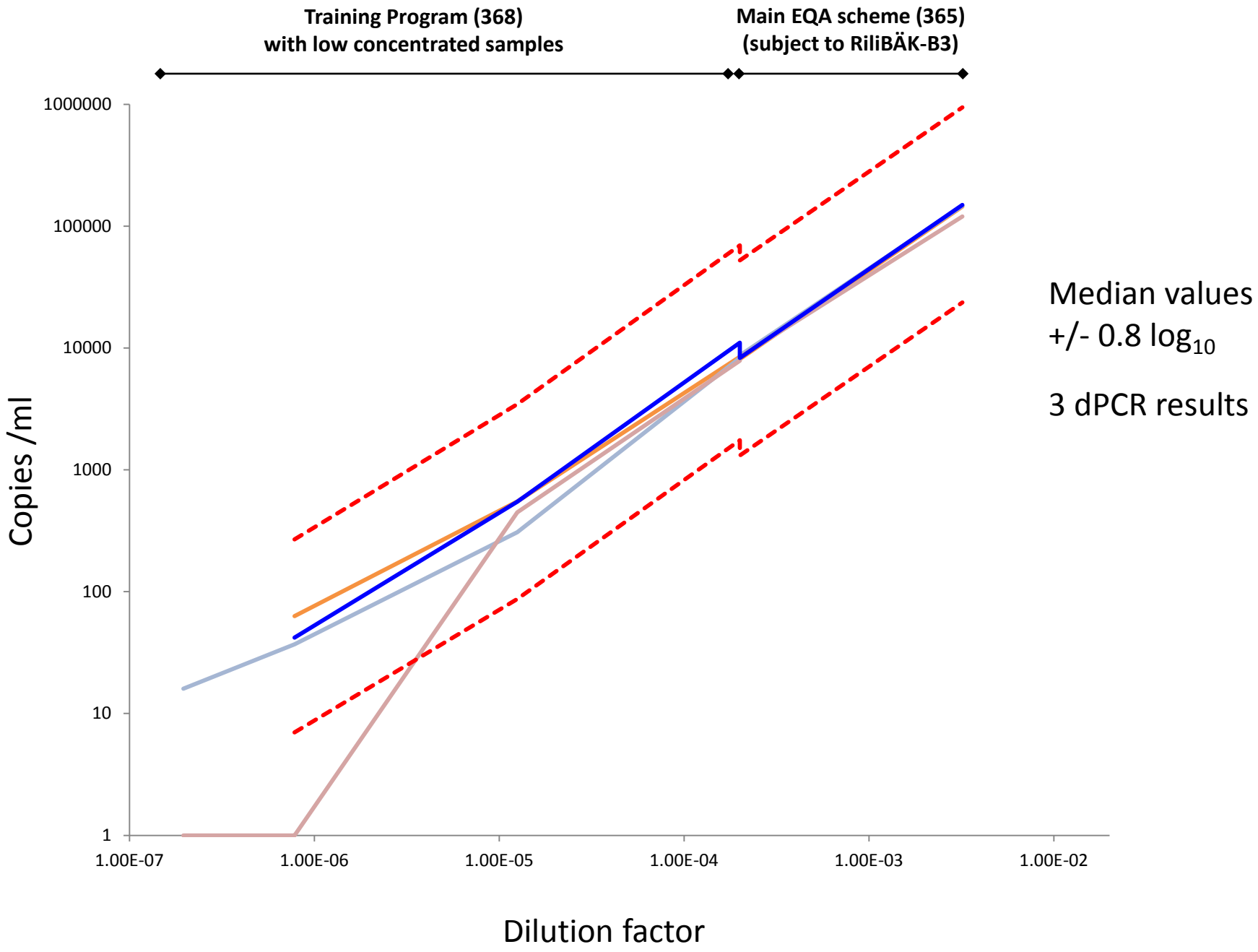
Dilution factor
Median values
+/- 0.8 log10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1.00E-05
1.00E-04
1.00E-03
1.00E-02
Dilution factor
Median values
+/- 0.8 log10
3 dPCR results

Quantitative CMV Genome Detection in Clinical Samples

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CMV Clinical Samples

Participant no.	**Lab A**	**Lab B**	**Lab C**	**Lab D**	**Lab E**	**Lab F**
PCR system	realtime	realtime	realtime	realtime	realtime	digital
Extraction						
Manufacturer	Qiagen	Roche	Qiagen	Roche	Roche	Roche
Kit name or Extraction System	QIA-Symphony	Magna Pure 96	QIAcube	High Pure Viral Nucleic Acid Kit	MagnaPure 96-DNA Viral Small Volume Kit	High Pure Viral Nucleic Acid Kit
Catalog no.	---	---	---	3502295001	---	---
Lot no.	---	10239500	148037934	10615300 (2016-01)	11295600	10343200
Performance	automatical	automatical	automatical	manual	automatical	manual
Amplification						
Manufacturer	in house	in house	Argene	Qiagen	in house	in house
Kit name	---	---	CMV R-gene	artus CMV LC PCR Kit	480 Probes master	---
Catalog no.	---	---	069-003 B	4503063	---	---
Lot no.	---	---	1003345350	148052697 (2016-03-12)	---	---
Thermocycler						
Manufacturer	ABI	Stratagene	Roche	Roche	Roche	BioRad
Name	7900 HT	Mx 3000P	LightCycler 2.0	LightCycler 2.0	LC 480	QX 100 Droplet Digital PCR System
Primer	UL 98 region	Polymerase gene	UL83 gene	MIE gene	Us 1+ region	UL 54
Probe	TaqMan	TaqMan	TaqMan	Eclipse hybridisation probe	TaqMan	Hydrolysis probe

Results												
Dimension	**IU/ml**	**Ct**	**Copies/ml**	**Ct**	**IU/ml**	**Ct**	**Copies/ml**	**Ct**	**Copies/ml**	**Ct**	**Copies/ml**	**Ct**	**Copies/ml**
	LOD 200 IU/ml		LOD 200 Copies/ml		LOD 500 IU/ml		LOD 600 Copies/ml		LOD 79 Copies/ml Quantification according to Qiagen kit		LOD 330 Copies/ml		
EMRP CMV Clinical Samples (in each case plasma)													
G10540 Pat. P. 1st donation (Mutation IE1-Ex4)	**100**	35,60	**100**	39	**250**	39	**3270**	39,16	**5650**	22,94	**196**	36,94	**555**
G10564	**10**	38,40	**below LOD**	---	**below LOD**	---	**109**	44,20	**835**	25,93	**50**	37,71	**2242**
G10575	**100140**	26,70	**800000**	---	**2000000**	---	**492000**	31,72	**184750**	17,47	**86600**	30,90	**341046**
G10576 Pat. P. 2nd donation (Mutation IE1-Ex4)	**10**	39,55	**below LOD**	---	**below LOD**	---	**neg.**	---	**805**	25,99	**18**	38,25	**150**
G10944	**50**	36,66	**500**	37	**1250**	37	**2650**	39,47	**5925**	22,86	**408**	36,49	**3213**
G11206	**8000**	29,83	**50000**	31	**125000**	31	**32400**	35,76	**24750**	20,62	**5580**	34,49	**20840**

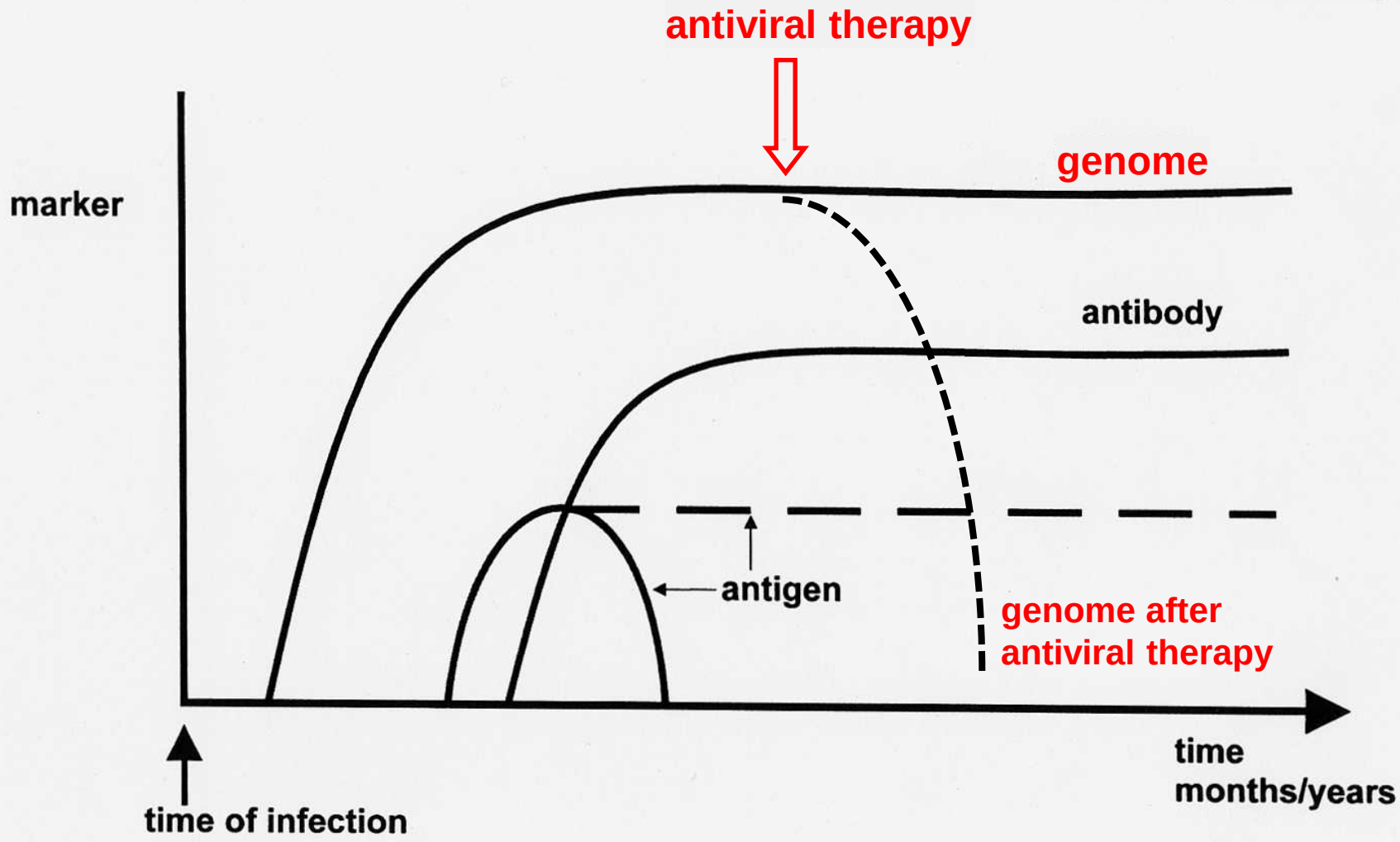
Factors influencing quantitative virus genome detection

- Extraction
- Amplification
- Detection
- Matrix -> commutability

➔ Standard/reference materials urgently needed
reflecting each of the steps/factors
real viruses in appropriate matrix

➔ Infectious disease diagnostics – no reference range !!!
analysis of dynamics

Generalised course of infection (TTIs)



JB/mm/8nov01(14)
micro/slides/dubai

Benefits of Quality Controlled and Standardized Diagnostics

Diagnostic data have to be solid and comparable irrespective of

- diagnostic laboratory
- diagnostic system
- staff

Correct diagnostic data

- are bases for
  - prevention
  - epidemiology – detection of re-/emerging infections
  - therapy
  - therapy monitoring / follow up
- lead to quality improvement of diagnosis
- protect the patient from false positive and false negative diagnostic results
- vigilance of the market (post-marketing surveillance)
- save money for health care system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search ID: rman1914
"Look, this diagnostic computer cost us $185,000.00! — if it says you're pregnant, you're pregnant!"

Partners in the EQA Network

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Vanessa Lindig
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INSTAND-Team
PD Dr. Oliver Donoso Mantke

München

Prof. Dr. Lutz Gürtler

and

35 INSTAND-Sollwert Laboratorien inkl.
Robert Koch-Institut
Paul-Ehrlich-Institut

Physikalisch-Technische Bundesanstalt (PTB)

and

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Thank you!

Univ.-Prof. i.R. Dr. Heinz Zeichhardt
Charité-Universitätsmedizin Berlin
Campus Benjamin Franklin - Institut für Virologie

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